THE UNIVERSITY OF TENNESSEE
MEMORIAL RESEARCH CENTER
KNOXVILLE

October 18, 1962

Dr. Joshua Lederberg
Stanford University
Stanford, California

Dear Dr. Lederberg:

This letter relates to an approach which seems to me to offer considerable possibilities in problems of genetically determined enzyme deletion, known in some instances to be occurring in problems such as that reviewed by the panel that you and Wendell Stanley were on concerning mental retardation. In such instances it would seem quite feasible particularly in degradative systems where it is known what enzyme is lacking, to infect the individual with a passenger virus known to carry information for the synthesis of the particular enzyme. This latter can be determined through simply taking cell lines in culture in which a deletion of the enzyme information has occured and infect them with a series of passenger viruses testing for the appearance of the enzyme. This sort of approach is one for a team type operation rather than for an individual investigation preferring to work with a small number of people such as myself. Such information derived might prove useful in a variety of diseases associated with operational or genetic enzyme deletion. In synthetic systems, I would not expect the chance of such an approach being useful as having any probability as the location of the enzyme in the cell would be expected to play a larger role. I am writing you concerning this as I do not know which particular organization might be interested, and I thought that if you felt the approach had possibilities you might pass it on. I discussed this recently with Lyndon Lee, who is Director of Research for the VA and it is possible that they may take on part of the problem.

My interest in this area stems from our findings with the Shope papilloma virus where we have determined that it is bringing in information for the synthesis of an arginase new to rabbit epithelium. It is at least in part responsible for the neoplastic state of the cells as when we by-pass the enzyme, the tumor growth is greatly slowed.

You may be more interested in a recent finding closer to your own work. There are two known lines of papilloma viruses, one is the wild type and is not recoverable from tumors of the domestic rabbit. The other is called the recoverable line and is recoverable as its name suggests. We have found that wild rabbit epithelium uses large amounts of serine. Wild rabbit papilloma and domestic rabbit papilloma

induced with the wild type virus also uses large amounts of serine. Domestic rabbit squamous epithelium, in contrast, uses rather little serine. Papilloma induced in the domestic rabbit squamous epithelium with the recoverable line uses proportionately little serine. Shope has found that if you put the recoverable line back in wild rabbits that it reverts to wild type. We are currently in the process of testing whether this reversion is associated always with this difference in serine metabolism and whether domestic rabbits carrying wild type virus induced papillomas make antibodies against an antigen found in virus-free wild rabbit epithelium. It seems quite possible that we are dealing with a piece of wild rabbit information incorporated in the wild type virus DNA - a situation not unlike you and Morse described with phage λ and Gal. I will let you know how this comes out.

With best regards.

Sincerely yours,

Stanfield Rogers

SR:srh